Original Article

Pre-prostatic tissue removed in robotic assisted lymph node dissection for prostate cancer contains lymph nodes

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Abstract

Objective: The on-going discussion about extent and best template for pelvic lymph dissection (PLND) motivated us to analyse pre-prostatic tissue (PPT) for lymph nodes and metastases.

Materials and Methods: From December 2010 to August 2011 PPT was sent for histopathological evaluation during 80 robotic assisted radical prostatectomies (RARP) and one extended staging lymph node dissection. All patients had either a limited (lPLND, $n = 44$) or an extended lymph node dissection (ePLND, $n = 36$). Clinical data were retrospectively analyzed and compared to histopathological findings.

Results: Lymph nodes were found in PPT in 10/80 (12.5%) patients after RARP and in the one patient after staging ePLND. Mean number of lymph nodes detected in PPT of them was 1.2 (range 1-3). Clinically no differences were found between patients with or without lymph nodes in PPT. In the standard template of either ePLND or lPLND the average number of lymph nodes was 13 (range 2-56). Herein metastases were found in 10 (12.5%) patients after RARP and in the patient after staging ePLND. A metastasis in PPT was only found after staging ePLND.

Conclusions: Pre-prostatic tissue might contain lymph nodes that potentially harbour metastases. In the intention to perform the most accurate staging this tissue should be considered for histopathological evaluation.

Key Words: Lymph nodes, prostate cancer, robotic assisted radical prostatectomy

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Received: 08.04.2012, **Accepted:** 12.06.2012

INTRODUCTION

For surgical reasons the anterior wall of the prostate is regularly freed from pre-prostatic tissue (PPT) during radical robotic assisted prostatectomy (RARP). Its removal allows a better visualisation of the pubic bone, the puboprostatic ligaments, the endoplevic fascia and the anterior bladder neck. Neither in open nor in robotic surgery is this tissue regularly sent for histopathological evaluation. Although extended pelvic lmyph node dissection (ePLND) is currently considered the gold standard of lymph node staging[1-3] and usually does not include peri-prostatic tissue, already Finely et al.[4] and Kothari *et al.*[5] reported the existence of lymph nodes in peri-prostatic tissue. Recently Yuh *et al.*[6] evaluated – overlapping to our study period- peri-prostatic fat for the presence of regional lymph nodes in 120 RARPs. In the present study this tissue was similarly evaluated with however, some differences in the surgical approach of PLND and time of tissue removal.

Access this article online	
Quick Response Code:	Website: www.urologyannals.com
	DOI: 10.4103/0974-7796.120301

MATERIALS AND METHODS

From December 2010 to August 2011 80 patients underwent RARP and one patient staging ePLND for prostate cancer at

our institution. In all patients PPT was removed and routinely sent for histopathological evaluation after PLND. PLND consisted either of a lPLND or an ePLND. Mean age of all patients was 63 years (range 50-77). In 44 patients a limited lymph node dissection (lPLND) defined by the obturator fossa and in 36 patients an ePLND defined inferiorly by the obturator fossa, laterally by the external iliac artery and cranially by the common iliac trunk with visualization of the ureter were performed. lPLND was performed in tumors characterized by PSA <10 ng/ml, Gleason <7a and clinical stage <2b. In all other tumors an ePLND was performed. All relevant clinical data were collected retrospectively by chart review.

Technically PPT was removed as follows: First the pubic bone and the anterior wall of the prostate were visualized. Then the puboprostatic ligaments were freed from the surrounding fatty tissue and the tissue layer was grasped by the assistant's forceps. The tissue was then carefully dissected from the anterior surface of the prostate towards the bladder neck [Figures 1 and 2]. Avoiding the obturator fossa the lateral borders of the field of dissection were carefully respected by the lateral edges of the prostate. The tissue was completely removed through the assistant's trocar. In case of a lPLND the lymphatic tissue from the right and the left obturator fossa was collected and separately sent for histophathological evaluation before removal of the PPT. If an ePLND was performed the lymphatic tissue also was collected before removal of the PPT from the regions of the obturator fossa, the external iliac artery and the common iliac trunk as well as both sides separately. All tissue samples were fixed in formalin and routinely embedded in paraffin. The tissue was evaluated for tissue size, microscopically for the presence and number of possible lymph nodes and if present for their size and dignity. All data were collected in an electronic database and statistically evaluated using JMP version 9.0 (SAS inc, Campus Drive Building S, Cary, NC 27513, USA). For comparisons of continuous data the students *t*-test was applied and for categorical data the chi square test. Data are presented as mean ± standard error of the mean (SEM) or as a range from maximum to minimum.

RESULTS

Specimen retrieval did not prolong surgical time as PPT was already routinely removed for a better visualization of the anterior wall of the prostate in previous surgeries. Its removal was considered especially in nerve-sparing procedures in which an apical release of the neurovascular bundles was performed of high importance. In this series the estimated time of PPT removal ranged from one to five minutes.

Table 1 shows the clinical pre- and post-operative data of patients in whom lymph nodes were found in PPT in comparison to patients without pre-prostatic lymph nodes.

Eighty-one PPT specimens from 81 patients were retrieved and sent for histopathological evaluation. The mean size of the tissue was 6.3 cm^2 (range 0.5-22). Tissue size did not correlate to prostate size, which was in mean 51 g (range 13-185 g). In lPLND the mean number of removed lymph nodes from the standard template was 8.6 (range 2-18). In ePLND it was 19 (range 7-53).

In ten patients after RARP (5 lPLND, 5 ePLND) and in the patient with a staging ePLND, lymph nodes were found in PPT ($n = 11$). The mean number of lymph nodes in this tissue was 1.2 (range 1-3). Their mean size was 5.5 mm (range 1-25 mm). Only in the patient with a staging ePLND a lymph node metastases was found in one out of two lymph nodes of PPT. The size of the metastasis was 6 mm in the longest diameter [Figure 3]. All other lymph nodes of PPT were negative for metastasis.

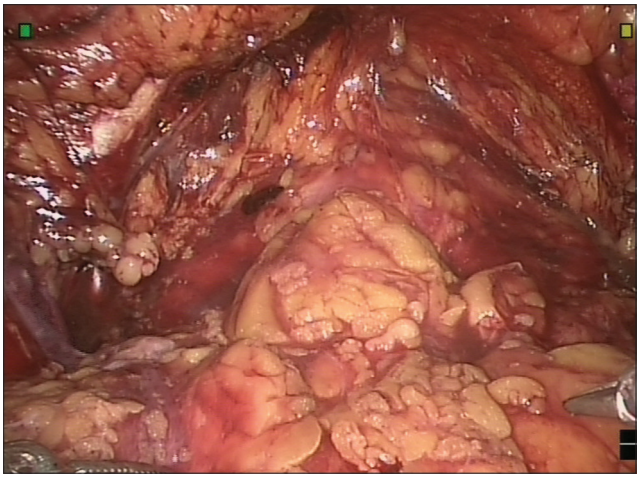

Figure 1: Pre-prostatic tissue prior to robotic removal during robotic assisted radical prostatectomy

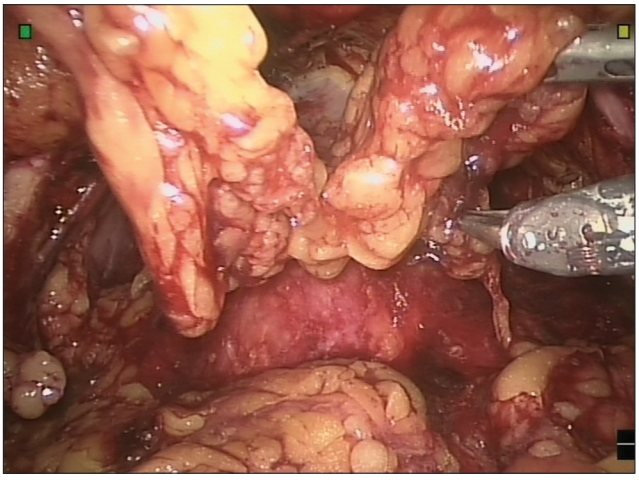

Figure 2: Robotic removal of pre-prostatic tissue during robotic assisted radical prostatectomy

In the template of either an lPLND or an ePLND, lymph node metastases were found in ten patients after RARP and in the patient with a staging ePLND. In this group of patients the mean number of removed lymph nodes was 19 (range 6-42) with in mean 2.6 (range1-9) lymph nodes harbouring metastases. Only in one patient after lPLND (n = 1/44, 2.3%) a lymph node metastasis was found in the standard template. In this patient one lymph node out of six harboured a lymph node metastasis with a diameter of 2 mm. In the group of patients with an ePLND and proven lymph node metastases (n = 9/36, 25%) the mean number of removed lymph nodes was 20.3 (range13-42) with in mean 2.7 (range1-9) positive lymph nodes. The mean diameter of metastases was 3.8 mm (range 1-17 mm). In the group of patients with lymph node metastases after RARP (n = 10) in the standard template no lymph node metastases were found in PPT. Only a benign lymph node was found in one of these patients in the respective PPT.

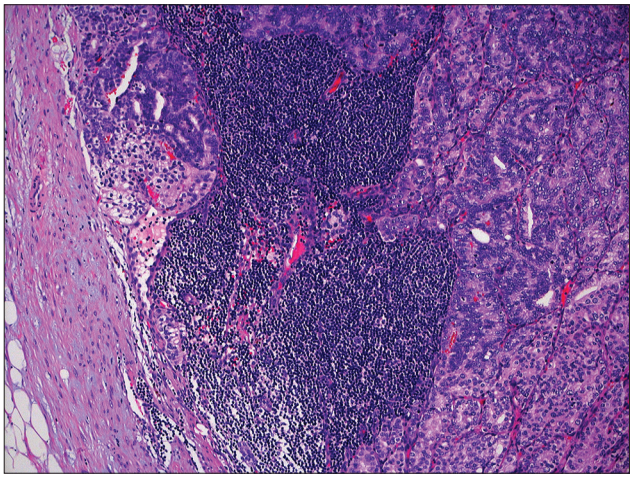

Figure 3: Lymph node infiltrated by metastatic prostate cancer

DISCUSSION

Advances in clinical imaging have improved the detection of lymph node involvement tremendously.[7] New techniques like combined ultra-small super paramagnetic particles of iron oxide-enhanced and diffusion-weighted magnetic resonance imaging seem to permit even a more sensitive radiologic imaging.[8-9] Still PLND remains the most accurate staging method in prostate cancer.[1] Although in some cancers like in bladder cancer an extended lymph node dissection is known to improve survival rates, the clinical benefit of patients with

Table 1: Pre- and post-operative data of patients in whom lymph nodes were found in PPT in comparison to patients without lymph nodes in PPT

	Patients with no lymph nodes in PPT	Patients with lymph nodes in PPT	*P* value	Patient with staging ePLND
Patients with and without lymph nodes in PPT (*n*=patients (%))	70 (86)	10 (12)		1 (1)
Nodes in PPT (*n*)	/	1.2 (1-3)		1
Size of LN in PPT (mm)	/	5.5 (1-22)		
Metastasis in PPT (n (size))	/	0		1 (6 mm)
Age (years)	64±0.8	62±2.0	0.35	65
BMI (kg/m^2)	25.8±0.5	27.2±1	0.32	24
Prostate size (ml)	50.0±3.0	58.4±7.4	0.35	50
PSA (ng/ml)	10.5±1.2	6.2±0.9	0.2	18
Biopsy gleason score (*n*=patients (%))			0.33	
<6	23 (33)	3 (30)		
7	33 (47)	4 (40)		
>7	14 (20)	3 (30)		1
Pathological gleason score (*n*=patients (%))			0.81	
<6	14 (20)	1 (10)		
7	47 (67)	8 (80)		
>7	9 (13)	1 (10)		1 (TURP)
P-Stage (*n*=patients (%))			0.43	
T2a	6 (9)	0 (0)		
T2c	44 (63)	8 (80)		
T3a	3 (4)	1 (10)		
T3b	17 (24)	1 (10)		Clinical stage T3b
Number of removed lymph nodes in PLND	13±1.0	17±2.9	0.4	14
lPLND (*n*=patients (%))	39 (56)	5 (50)		/
Number of lymph nodes in lPLND (*n*)	8±0.6	9±1.8	0.37	/
ePLND (*n*=patients (%))	31 (44)	5 (50)		1
Number of lymph nodes in ePLND (*n*)	18±1.7	24±2.9	0.09	14
Positive LN in PLND (*n*=patients (%))	9 (13)	1 (10)		1
Number of positive LN in PLND (*n* (range))	2.66 (1-9)	1		3
Mean size of metastases (mm (range))	4 (1-17)	2		5 (1-7)

PPT: Pre-prostatic tissue, PLND: Pelvic lymph dissection, BMI: Body mass index, PSA: Prostate specific antigen,LN: Lymph nodes

prostate cancer remains discussed. It is however, common sense that positive lymph nodes are one of the strongest predictors of disease recurrence.[2] Because the clinical benefit of PLND remains doubtful[1] and has a well described morbidity that increases with extend, different concepts of lymph node removal are proposed. Some urologic surgeons avoid lymph node dissection in patients with low risk cancers,[1] others propose sentinel node techniques to actively detect atypical lymph nodes.[3,10] Again others follow the concept of a lPLND or an ePLND dissection according to clinical stage as recommended by the current EAU guidelines[1,2] and as it was performed in the present study.

However, in none of the techniques the removal of PPT for lymph node staging is described. Even though most lymphatic drainage happens through the obturator fossa and is covered by a lPLND,[11] about 19-35% of sentinel lymph nodes were detected in a recent study by Schilling *et al.* outside this template.[3] However, in this evaluation the pre-prostatic region was not mentioned as a possible route of lymphatic drainage. Still with the more and more widespread use of robotic surgery this tissue turned into the focus of discussion as it is regularly removed for a better visualization of the prostate and the bladder neck.

Recently Yuh *et al.* published their series of 120 patients in whom in 20 patients after RARP lymph nodes were detected in PPT (16.7%).[6] In their series no pre- and post-operative differences regarding Gleason Score/stage/PSA between both groups of patients were reported. Also the present study revealed lymph nodes in PPT but in a lower percentage of patients (12% vs. 16.7%). If detected the mean number of pre-prostatic lymph nodes was equal in both studies (1.2 vs. 1.5). As a possible explanation for the slightly higher number of patients with lymph nodes in PPT we consider the fact that PPT was removed in the study by Yuh *et al.* always prior[6] and in the present study always after PLND to be important. This might have led to a gain of removed tissue in contrast to the present study in which the standard lymph node dissection was already performed. Furthermore, Yuh *et al.* performed PLND only in 64 (53%) of their patients, whereas in the present study it was performed in all.

Similar to the study of Yuh *et al.* the presence of lymph nodes in PPT was in the present study independent of clinical parameters like tumour stage, Gleason score and PSA levels. Only a slight tendency to more removed lymph nodes in the standard regions of PLND was found in patients in whom PPT contained lymph nodes than in those in whom PPT did not contain lymph nodes (13 vs. 17 lymph nodes, P = n.s).

Whereas lymph node metastases were found by Yuh *et al.* in 3 out of 20 (15%) patients,[6] in the present study PPT contained a lymph node metastases only in one patient with advanced disease after an extended staging PLND (1 patient out of 11 (9%)). This again may be related to the fact that in the present study PLND was performed in all patients, whereas by Yuh *et al.* only in 64 patients (53%) with in mean only 7 removed lymph nodes.[6] In the three patients in whom pre-prostatic lymph node metastases were found by Yuh *et al.*, 4, 5 and 9 lymph nodes were detected in their standard PLND. This corresponds in comparison to the present study rather to the average of lPLND than of ePLND. Therefore it remains possible that, if in these patients an ePLND would have been performed, additional lymph node metastases might have been detected. This of course limits the exclusivity of the detected pre-prostatic lymph node metastases by Yuh *et al.*

In the present evaluation the number of patients with lymph node metastases in the standard template was high (10%) and in contrast to that the number of patients with PPT lymph nodes (n = 10) or metastases (n = 1) low. Even though in the present work no lymph node metastases were found in PPT of the main reference group, its possibility was confirmed by a single patient. The fact that otherwise no lymph node metastases were found in the present study in PPT has according to our opinion to be mainly attributed to the small size of the cohort (n = 80).

As a summary in line with the current literature the present study confirmed the presence of lymph nodes to an equal extend and amount in PPT as described before. Whereas in other series exclusive lymph node metastases were describe, this could not be shown here. Still the possibility of lymph node metastases in PPT was confirmed and similar to other studies clinical parameters did not predict the presence of lymph nodes in PPT.

With further evidence of the present study that pre-prostatic tissue contains lymph nodes we conclude that histopathological evaluation of pre-prostatic tissue is worth considering if the most exact staging is the surgical aim. This seems to be justified as its removal neither increases morbidity nor surgical time.

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How to cite this article: Blarer J, Padevit C, Horton K, Pfofe D, John H, Horstmann M. Pre-prostatic tissue removed in robotic assisted lymph node dissection for prostate cancer contains lymph nodes. Urol Ann 2013;5:259-63.

Source of Support: Nil, **Conflict of Interest:** None.